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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/493,427	01/29/2000	Patrick L. Iverson	0450-0025.30	2225

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EXAMINER

EPPS FORD, JANET L

ART UNIT	PAPER NUMBER
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1633

DATE MAILED: 12/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/493,427	Applicant(s) IVERSON ET AL.	
	Examiner Janet L. Epps-Ford	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 28,32-41 and 45-49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 28,32-41 and 45-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 January 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 28, 32-41, and 45-49 are presently pending.

Response to Arguments

Claim Rejections - 35 USC § 103

2. Claims 28, 32-41, and 45-49 remain rejected under 35 USC 103(a) as being unpatentable over Zalewski et al. (US Patent No. 6,159,946) in view of Kobayashi et al., Summerton et al. (US Patent No. 5,378,841), Burger, and Agrawal et al. for the reasons of record set forth in the Office Action mailed 3-19-04, and those reasons set forth below.
3. Applicant's arguments filed 9-23-05 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that overall, none of the cited references provide any guidance or expectation of success of suppression of restenosis in a human patient. Applicants have based this assertion on the observations set forth in the Weller Declaration submitted on May 1, 2003, and the post filing Kutryk et al. (2002) reference.

Contrary to Applicant's assertions, the substance of the Weller Declaration is essentially an optimization of what was previously known in the prior art. At the time of the instant invention, the prior art described the use of modified antisense targeting c-myc, having the sequence of SEQ ID NO: 1 (Kobayashi et al. and Zalewski et al.), for use in the treatment of restenosis in a patient (Zalewski et al.), the benefits of modifying antisense to comprise an uncharged morpholino backbone, including those comprising a phosphorodiamidate linkage (see Summerton et al. col. 25, Example 8, "C" wherein

Art Unit: 1633

X= --N(CH₃)₂), and the use of morpholino modified oligomers for the treatment of restenosis (Burger), wherein the administration to humans for the treatment of restenosis is disclosed (page 10, lines 10-24, teaches that optimum dosages for a given route in a human can be determined by routine experimentation).

Applicants have not provided any evidence *that at the time of the instant invention*, that it would not have been obvious to modify the teachings of the phosphorothioate modified antisense compound of Zalewski et al. with the teachings of Summerton et al. or Burger in the design of morpholino modified antisense compounds for the treatment of restenosis, for the known benefit of conferring better target inactivation in comparison to conventional antisense, due to the greater binding affinity, and enhanced cellular uptake (see Burger, page 7, lines 27-32; and Summerton et al., col. 16, lines 22-49). Due to the efficacy of the phosphorothioate modified anti-*c-myc* antisense as observed in the porcine model of Zalewski et al., there is no evidence of record that at the time of the instant invention, why one of ordinary skill in the art would not have had a high expectation of success for the *in vivo* use of a morpholino modified antisense compound, having the same sequence, targeting *c-myc*, for the treatment of restenosis, since morpholino modified oligomers are known in the art as having enhanced properties over conventional antisense compounds.

Applicant's reliance upon a post-filing references, Bult et al. (July 2000), Gruberg et al. (November 2000), Kent et al. (2004), and Kutryk et al. (2002), and post-filing data, the Weller Declaration, to support the assertion that there was no expectation of success of making and using the invention produced from the combination of the cited

Art Unit: 1633

references is improper based upon 35 USC § 103(a), which states that “...if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious **at the time the invention was made** to a person having ordinary skill in the art to which said subject matter pertains.” Contrary to applicant’s assertions, there is no evidence of record that would suggest that at the time of the instant invention it would not have been obvious to use an antisense compound having the sequence according to SEQ ID NO: 1, wherein said sequence comprised the morpholino modifications as recited in the claims for the treatment of restenosis in a patient. Contrary to Applicant’s assertions, the basic or essential elements of the claimed invention are disclosed in the prior art, and that it would have been obvious to vary the general conditions (e.g. dosage, see Burger page 10) in a method of treating restenosis in an effort to optimize results.

Although Applicants argue that the therapeutic approach described by Burger targets a distinct nucleic acid target, contrary to Applicant’s assertions, the teachings of Burger teach the ordinary skilled artisan how to treat the same particular tissues treated in the instant claims for the same condition, namely restenosis, comprising the administration of morpholino modified antisense compounds. The disclosure of Burger provides specific guidance for the treatment of restenosis in a human patient comprising the administration of a morpholino modified antisense compound. Although Burger focuses on antisense compounds targeting CMV, the prior art, Zalewski et al. provides express motivation for the treatment of restenosis comprising the use of the antisense compound according to SEQ ID NO: 1 of the present invention. Burger teaches the

Art Unit: 1633

efficacy of morpholino modified antisense compounds for the treatment of restenosis. As stated above, the application of rejections under 35 USC 103(a) address what the ordinary skilled artisan would have considered obvious at the time the instant invention was made, based upon the totality of the prior art, not based upon what was demonstrated after the filing date of the instant invention.

It is noted that the optimized amount of oligomer for use in the treatment of restenosis in a human was first identified in *preclinical pig* studies as being at or near the optimal therapeutic dose, see page 2, 4th paragraph of Weller Declaration. The Zalewski et al. reference also uses a porcine model to make predictions regarding the use of antisense compounds for the treatment of restenosis in mammals, generically (see claims). Contrary to Applicant's assertions, at the time of the instant invention the disclosure of Burger and Zalewski et al. provided sufficient guidance for the skilled artisan to practice the full scope of the claimed invention. Therefore, it remains that the invention as a whole would have been *prima facie* obvious Zalewski et al. (US Patent 6,159,946) in view of Kobayashi et al., Summerton et al., Burger, and Agrawal et al. at the time the instant invention was made.

Claim Objections

4. Claims 28, 38, and 41 are objected to because of the following informalities: The formula recently introduced in the claims does not provide a definition for the terms P_i and P_j as recited in the formula. Appropriate correction is required.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 9:30 AM through 6:30 PM.

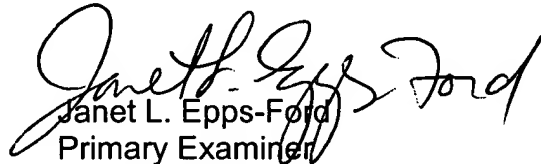
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 517-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Art Unit: 1633

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Janet L. Epps-Ford
Primary Examiner
Art Unit 1633